FURTHER RESEARCH ON CHEMICAL CONTRACEPTION*

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THE work on chemical contraception done under my direction in the Sir William Dunn School of Pathology at Oxford is financed by the Birth Control Investigation Committee, part of whose funds are derived from the *Eugenics Society*. For eight years I have benefited from the advice and encouragement of Dr. C. P. Blacker. My co-workers are Dr. H. M. Carleton, who confines his attention to the pathological side of the research, Mr. R. M. Ranson and Mr. J. Tynen. Most of our work may be classified under four heads: the study of the scientific basis of chemical contraception; the invention of good chemical contraceptives; the testing of proprietary products; and the making of reports on semen specimens submitted by patients.

Nomenclature

The naming of chemical contraceptives is rather confused, and I wish to suggest the following classification, based on the nature of the vehicle in which the contraceptive is dissolved or suspended. The words are logical extensions of terms commonly used in pharmacy, chemistry and physics.

The product may be solid, semi-liquid or liquid at room temperature. If it is solid, we may call it a suppository, and of this there are three kinds: the gel or jelly suppository (usually with gelatine as a vehicle); the fatty suppository (often with cocoa-butter); and the tablet suppository (including the types which produce a foam on contact with water). The semi-liquid products, which can be squeezed from a collapsible tube, are pastes, mucilages and ointments. Pastes are thick aqueous products, without any considerable admixture of gums, and the word is particularly applicable when starch is present. Gelatine is often present in these in the sol condition, and the name "jellies" has been used loosely for such products. This is most confusing, for the word gel or jelly is only properly applicable to an elastic solid, such as a gel suppository. (A few of our own research products are just solid and elastic at room temperature, but can be squeezed from a tube, and we call this limited type "tube-jellies.") If an aqueous semi-liquid has a considerable content of gum, we may call it a mucilage. If the product is non-aqueous, but owes its semi-fluidity to a fat or other substance insoluble in water, we speak of an ointment. If the vehicle is wholly fluid, we speak of a douche.

Pastes may be used in two different ways: either smeared on the upper (cervical) side of a rubber occlusive pessary before the latter is inserted in the body, or inserted by some mechanical means in the vagina shortly before coition. In our opinion these two uses require different properties in the product, and we suggest that pastes should be called cervical or vaginal, according to their intended uses.

Gel and fatty suppositories dissolve or melt at the temperature of the body, and are therefore unsuited for use in the tropics. It is likely that vaginal pastes, in collapsible tubes, will become the simplest means of chemical contraception in hot climates, though gel suppositories may be transported to tropical uplands in refrigerating vans.

Simplicity and Complication

In our own country, elaborate methods of contraception are often advised. The woman has to smear a cervical paste or ointment over a rubber pessary and insert it before retiring to bed, without knowing whether it is going to be required or not. If coition occurs, a suppository is inserted. Next morning the vagina is washed out with a douche and the pessary removed, cleaned, dried and put away. This elaborate technique

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may be all right for some women, who are very painstaking and have the necessary privacy and bathroom accommodation, but even for these the necessity to take precautions without knowing whether they will be needed is irksome. For the majority of women these complications are a great difficulty, and for poor women, with almost no privacy and no proper bathroom accommodation, they are impossibilities. The existence of complicated methods of contraception will not prevent the innately careless and foolish woman from having many children, while the innately careful and far-seeing ones produce fewer offspring. This will have a dysgenic effect, and thus the discovery of a really simple but effective method is of eugenic importance.

Our work has definitely eugenical significance also in quite another way, for we are investigating also the methods of stimulating sperms to greater activity, and this may be useful in promoting the fertility of certain eugenically desirable people.

The only contraceptive that can be used just when required and which needs no mechanical help for insertion is the suppository. The fatty suppository has the disadvantage that the spermicide diffuses out too slowly, while the tablet may not dissolve sufficiently quickly if the vagina is dry. The gel suppository cannot fail to become fluid if it is properly designed, and the spermicide is in solution in it, ready for immediate action. If the spermicide is a really powerful but harmless one, a very convenient method of contraception is thus available. I claim that chemical contraception has never really been tried, because there has not been a powerfully spermicidal gel suppository on the market. Until it has been tried, we cannot be certain that chemical methods alone, without any occlusive pessary, are necessarily unsafe. It has not been definitely proved that the human uterus cannot suck up sperms from the vagina ; but if it can do that, it cannot fail to suck up the spermicide also.

Tests of Spermicidal Power

We have designed a series of rather complicated laboratory tests for telling us how likely a given product is to achieve its purpose. In designing these tests we have had the advantage of being able to discuss them with the very experienced clinical workers who constitute the medical subcommittee of the National Birth Control Association. My first tests were designed eight years ago and seem very primitive now, but we have profited from criticism and are using a set of tests which are, I believe, about as good as laboratory tests ever will be. I greatly hope that the medical profession will accept them as guides to the choice of suitable products. A full description of our tests will be published in the *Journal of Hygiene*, and only a brief mention of them is allowable here.

We first test the rate of disintegration of a suppository. This test is obviously not applicable to an already semi-liquid paste, mucilage or ointment. We next titrate to find the amount of acid or alkali present. It is a strange fact that nearly every product on the market is acid. The vagina is probably usually acid, and no doubt people have thought it best not to change the reaction ; but this is really a very thoughtless dogma, for the vagina normally receives semen and cervical secretions, both of which are alkaline. No damage is likely to accrue from weakly alkaline or acid chemical contraceptives on account of their alkalinity or acidity, and alkaline products would perhaps be particularly suitable for cervical pastes and ointments.

The next test is that of total spermicidal power on human sperms in alkaline solution. This test shows how much spermicidal power can be extracted from the product. We postulate that in normal circumstances there are 6 c.c. of fluid in the vagina after coition, and our standard (S) concentration is therefore one suppository or one dose (2 grams) of a paste or ointment to 6 c.c. of sperm suspension. There ought to be a margin of safety, and we therefore do tests also at weaker concentrations of the spermicide ($\frac{S}{2}$, $\frac{S}{4}$, $\frac{S}{8}$, etc.). Observations on the activity of the sperms are made at five and thirty minutes. The test is also performed in an acid medium, since the contents of the vagina may be

slightly acid after coition, and some spermicides are less effective in acid solution. The next test is the extremely important diffusion test, which measures not the total amount of spermicidal power that can be extracted from the product, but the rate of diffusion of the spermicide out of the (already disintegrated) vehicle into the semen. Observations are made at 2, 5, 15, 30, 60, 120 and 180 minutes. This test is exposing the reason for the ineffectiveness of chemical contraceptives used alone, for although enough spermicide is sometimes present, it generally remains uselessly in the vehicle and does not come into contact with the sperms. This particularly applies to pastes and ointments.

The Pathological Test

The pathological test is on bitches, which were chosen on account of the general histological resemblance of the vagina to the human one. The organ is much larger than one would expect from the relative body sizes of bitch and woman, and we think it fair to make the dose half a suppository (or half the normal dose of a paste or ointment). We introduce half a suppository into the bitch's vagina daily for a fortnight, and then kill the bitch and make microscopical sections of the vagina, which are examined by Dr. Carleton.

Pregnancy Rate

Any product which comes out well in our tests is suitable for clinical trial. It is naturally essential that a good contraceptive should work well in practice, though it is probable that failures will never be completely eliminated, for people will always exist who will fail to carry out even the simplest instructions.

When it is desired to compare the efficiency of different contraceptives in practice, clinical workers should give information which will make it possible to calculate the pregnancy rate for each method. The pregnancy rate is the number of pregnancies per 100 ovulations, i.e. $\frac{100P}{V}$ where P is the number of pregnancies (whether full-term or abortions) and V is the number of ovulations at which conception might have occurred or did occur. $V=M-A+P$, where M is the number of menstruations (i.e. the number of ovulations not resulting in pregnancy); A is the number of times that the husband is absent from his wife during one whole menstrual cycle (starting at any point in the cycle), at a time when his wife is menstruating regularly; and P is the number of pregnancies (i.e. the number of ovulations resulting in pregnancy). When exact data for M and A are not available, one may allow thirteen menstruations to the year. It is not possible to make allowance for the number of menstrual cycles in which, for one reason or another, coition did not occur during the most fecund period, mid-way between two menstruations. The most convenient way in which to write the formula for pregnancy rate is $\frac{100P}{M-A+P}$.

When ovulation starts again after pregnancy, there may be some lack of correspondence with menstruation, but probably not enough to influence the results greatly. Clinical workers must be careful to get information as to when menstruation starts again after a full-time pregnancy or abortion (if indeed it does occur before the next pregnancy). Pearl* allowed only 0·04 year for the puerperal state in his calculations of the pregnancy rate of over 30,000 women, the details of whose menstruations were not known; but clinical workers will probably be able to get the necessary information. They should confine their studies to married women and should report the values of M, A and P for each woman separately. Pearl† has shown that where no contraceptive device is used the pregnancy rate is considerably higher up to the age of twenty-four (except that girls of fourteen and less who become pregnant have a low rate). It would therefore be best to divide married women into two groups, namely those less than twenty-five years old, and those aged twenty-five to thirty-nine. It would be best to exclude women aged forty and over. I suggest only two age groups, because probably only a

* *Lancet*, 1933, II, 607.

† *Milbank Memorial Fund Quarterly*, 1936, XIV, 1.

rather small number of women will agree to test one contraceptive consistently and to give information on their menstruations, pregnancies, abortions, etc. Individual women will, of course, pass from one age group to the other if they become twenty-five years old during the period of observation.

Pearl's figures, arrived at in a slightly different way, indicate that if a contraceptive were having any effect at all one should expect a mean pregnancy rate of less than sixteen for the younger age group and less than eleven for the older. The figures given (sixteen and eleven) are roughly those for American white women when contraceptives are not used.

Reports on Semen Specimens

We make routine examinations of the semen of two classes of patients of clinical workers, namely men who fear they may be sterile, and those who fear that their sperms are particularly resistant to spermicides, so that they present particular difficulties for chemical contraception. We have shown that there are men with unusually resistant sperms. We report on the volume of the specimen, the number of sperms per c.c., their activity, resistance to spermicides, and abnormalities in structure (if any), the pH of the semen and its buffering power against acids, and the presence in it of crystals, prostatic concretions, and cells other than sperms.

Conclusion

In conclusion, I want to say that I am hopeful that our research will result in the discovery of a reliable chemical contraceptive, and that this *Society* will consider that it has served the cause of eugenics by supporting our work.